PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
SCB/50965001		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB99/02241	14/07/1999	14/07/1998
International Patent Classification (IPC) or national classification and IPC		
C12N15/52		
Applicant		
JANSSEN PHARMACEUTICA N.V. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
18/01/2000	19.12.2000
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Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/02241

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:
Description, pages:

1-63 as originally filed

Claims, No.:

1-48 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under Item 1 and annexed to this report.)

6. Additional observations, if necessary:

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

   ☐ restricted the claims.

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:
   see separate sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

   ☒ all parts.

   ☐ the parts relating to claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2-4, 6, 8, 11, 13, 14
	No:	Claims	1, 5, 7, 9, 10, 12, 15, 18-48
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-48
Industrial applicability (IA)	Yes:	Claims	1-48
	No:	Claims	

2. Citations and explanations
see separate sheet

Re Item IV

Lack of unity of invention.

The present patent application refers to three members of the NAALADase group of peptidases. Specifically, full-length human NAALADase-L, and two previously unidentified members of the gene family, termed NAALADase-II and NAALADase IV, were isolated from human cDNA.

The common technical feature (Rule 13.2 PCT) to the genes and proteins subject of the current application, is that they belong to the family of NAALADases.

This feature, however, does not define a contribution over the prior art, since several members of NAALADases were already defined in the prior art (document D1, abstract; document D2, and references therein). Thus, since the common technical feature of the inventions claimed in the application is not inventive, unity of invention is compromized.

The claims of the current application are therefore regarded as referring to three different inventions:

I) human NAALADase-L, Claims 1-4, 10-11, as well as (all partially) 9 and 18-48
II) NAALADase-II, Claims 5-6, 12-14, as well as (all partially) 9 and 18-48
III) NAALADase-IV, Claims 7-8, 15-17, as well as (all partially) 9 and 18-48

Since, however, the examination of these different inventions poses no excessive effort, no invitation to restrict or to pay additional fees is extended at the moment.

Re Item V

Reasoned statement under Art. 35(2) PCT with regard to novelty, inventive step or industrial applicability.

The application does not meet the requirements of Art. 33 PCT since **claims 1, 5, 7, 9, 10, 12 and 15 are not novel**, and **claims 1-48 do not appear to contain an inventive step.**

1) Reference is made to the following documents (the document numbering corresponds to their order of citation in the international search report):
D1: SHNEIDER, B.L., ET AL.: "Cloning and characterization of a novel peptidase from rat and human ileum." J.BIOL.CHEM., vol. 272, no. 49, 5 December 1997, pages 31006-31015, XP002129302
D2: LUTHI-CARTER R, ET AL.: "Isolation and characterization of a rat brain cDNA encoding glutamate carboxypeptidase II" PROC.NATL.ACAD.SCI. USA, vol. 95, March 1998, pages 3215-3220, XP002129303

Novelty.

2) The scope of claim 1 extends to a cDNA molecule encoding human NAALADase-L, or a functional equivalent thereof.

In lack of a precise definition of a function which distinguishes human NAALADase- L from the NAALADases already known in the prior art, a similar function is assumed on the basis of protein homology. Vice versa, the known forms of NAALADase-I (D2, entire document, and references therein), as well as rat NAALADase-L (D1, entire document), can be regarded as functional equivalents of human NAALADase-L.

Since this is comprised in the subject-matter of claim 1, this claim can not be regarded as being novel.

The same applies to the related claim 10, which refers to the human NAALADase-L protein itself, or a functional equivalent thereof.

3) For the same reasons, the NAALADases known in the prior art can be regarded as functional equivalents of NAALADase-II and NAALADase-IV. Therefore, claims 5 and 12, and claims 7 and 15, the scope of which extends to functional equivalents of NAALADase-II and NAALADase-IV, respectively, cannot be considered to be novel.

4) However, claims 2 - 4 and 11, which refer more specifically to a precise nucleotide or amino acid sequence of human NAALADase-L or splice variants thereof, neither of which have been disclosed entirely in the prior art, can be considered to be novel.

For similar reasoning, claims 6, 13 and 14, and claims 8, 16 and 17, which refer to specific nucleotide or amino acid sequences of human NAALADase-II and human NAALADase-IV, respectively, are regarded as being novel.

5) Besides the fact that claim 9 also may depend on the claims 1, 5 and 7, all of which lack novelty, the scope of this claim also lacks a precise definition, since a minimal length of the nucleic acid molecule subject of the claim is not given. It may thus be understood as being limited to a sequence of one or few bases, which have doubtlessy been disclosed in the prior art.
This claim therefore also lacks novelty.

6) Novelty of the claims 18 - 48 can only be examined if novelty of all claims they depend on has been restored.

Inventive Step.

7) The genes and proteins for human, rat and murine NAALADase-I, and for rat NAALADase-L, were known in the prior art. Also, a cDNA fragment encoding roughly half of human NAALADase-L was described.

The technical problem therefore was the identification of new genes and proteins with similar properties.

The obvious solution to the person skilled in the art would be the identification of genes related to the known NAALADases, by sequence comparison and standard cloning thechniques.

The solution of the present patent application is the provision of human NAALADase-L, human NAALADase-II and human NAALADase-IV.

The identification of the genes was performed by the inventors as follows:

human NAALADase-L:

- With the sequence information from the prior art, PCR primers for the 3' end of human NAALADase-L were designed.
- PCR was performed using commercially available cDNA as template.
- To obtain the 5' end of the gene, a RACE assay was performed using a standard kit.

human NAALADase-II:

- With all sequence informations on NAALADases from the prior art, BLAST searches on EST databases were performed.
- Positive clones were ordered and sequenced. One of them contained an entire reading frame coding for a protein, which was designated NAALADase-II.

human NAALADase-IV:

- Sequence information from another positive EST clone revealed a partial coding sequence of another NAALADase. This sequence was used in a second BLAST comparison to EST databases.
- The resulting sequence information yielded a contig encoding a protein, which was designated NAALADase-IV. Isolation of the entire gene was performed by PCR.

The isolation of these genes has thus clearly been performed by standard methods used in the field, and was based on sequence information of the known NAALADases.
Since moreover the new NAALADases do not seem to show a surprising effect, the identification and isolation of the genes and proteins therefore lacks an inventive step.

Thus, claims 1-8 and 10-17, which refer to the NAALADases subject of the application, and to the nucleic acids encoding said NAALADases, are regarded as not complying with Art. 33(3) PCT.

8) Dependent claims 9 and 18-48 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step.